

P R A C E O R Y G I N A L N E
położnictwo

Pregnancy-dependent blood flow velocity changes in lower extremities veins in venous insufficiency

Zmiany prędkości przepływu krwi w naczyniach żylnych kończyn dolnych w ciąży powikłanej niewydolnością żylną

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Abstract

Introduction: Venous insufficiency in pregnancy is associated with an increased risk of complications.

Objectives: The aim of the study was to analyse the venous system changes of the lower limbs during pregnancy and puerperium with or without venous insufficiency.

Material and methods: The research was carried out on pregnant women divided into two groups according to the presence or lack of venous insufficiency. The venous system was examined four times: between 11-14th, 18-22nd, 28-32nd gestational week and at the 6th week of puerperium. The doppler examination included the measurement of the blood flow velocity in selected deep veins of the lower limbs: common femoral vein, the superficial femoral vein and the popliteal vein. Consecutively, the changes in the blood flow velocity during pregnancy and puerperium were compared between groups and finally to the results obtained in the 1st trimester.

Results: The analysis of the blood flow showed that the blood flow velocity was statistically lower in the group with venous insufficiency. Velocity changes in time showed, in majority of cases, a substantial reduction in the blood flow velocity in the third trimester in both groups. This blood flow velocity increases during the puerperium and does not differ from those observed in the first trimester. Thus, the tendency of changes in the blood flow velocity were similar in character in both groups.

Conclusions: The pregnancy related changes in venous system of lower extremities showed the reduction of blood flow velocity with advancing gestational age and were more evident in pregnancy complicated by venous insufficiency.

Key words: **pregnancy / blood / velocity / venous insufficiency / Doppler /**

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Streszczenie

Wstęp: niewydolność żylna w ciąży związana jest ze zwiększonym ryzykiem powikłań.

Cele: Celem pracy była analiza zmian w układzie żylnym kończyn dolnych w czasie ciąży i porodu, z lub bez niewydolności żylny.

Materiał i metody: Badania przeprowadzono wśród ciężarnych, które podzielono na dwie grupy w zależności od obecności lub braku niewydolności żylny. Układ żylny badano czterokrotnie: między 11-14, 18-22, 28-32 tygodniem ciąży oraz w 6. tygodniu porodu. Badanie dopplerowskie obejmowało pomiar prędkości przepływu krwi w wybranych żyłach głębokich kończyn dolnych: wspólnej żyły udowej, powierzchownej żyły udowej i żyły podkolanowej. Kolejno, zmiany prędkości przepływu krwi w okresie ciąży i porodu porównano między grupami oraz do wyników uzyskanych w 1 trymestrze ciąży.

Wyniki: Analiza przepływu krwi wykazała, że prędkość przepływu krwi w badanych naczyniach była statystycznie niższa w grupie z niewydolnością żylną. Zmiany prędkości przepływu w czasie wykazały, w większości przypadków, znaczne zmniejszenie prędkości przepływu krwi w trzecim trymestrze ciąży w obu grupach. W okresie porodu obserwowano wzrost prędkości przepływu krwi do wartości nieróżniących się od tych obserwowanych w pierwszym trymestrze. Tendencja zmian prędkości przepływu krwi była podobna w obu grupach.

Wnioski: Zmiany układu żylnego kończyn dolnych związane z ciążą wykazały zmniejszenie prędkości przepływu krwi w zaawansowanym wieku ciążowym i były bardziej widoczne w ciąży powikłanej niewydolnością żylną.

Słowa kluczowe: niewydolność żylna / doppler / układ żylny / ciąża /

Abbreviations

- CEAP – Clinical severity, Etiology or cause, Anatomy, Pathophysiology
– venous disease of the legs classification
- CFV – common femoral vein
- DVT – deep vein thrombosis
- L – left side
- PV – popliteal vein
- R – right side
- SFV – superficial femoral vein
- VI – venous insufficiency

The reasons for increased incidence of chronic venous insufficiency (VI) in women are very complex. In the pathophysiology of the venous system, special attention is paid to the muscles and lipid tissue enclosing the blood vessels of the lower limbs. The tissue surrounding the vessels is in women closely connected with the muscles and fascial spaces. The growing uterus is the mechanical factor, which is compressing the venous plexuses of the small pelvis, can also compress the inferior vena cava, causing impaired venous return to the heart, and thus weaken the value of suction force [1, 2]. The other factor is the increasing plasma volume in the pregnant women. It causes the greater pressure on the walls of the vessels, which can cause in return its weakening, relaxation and the development of the venous insufficiency. The major factors causing changes in blood vessels in pregnancy include hormonal changes that are the part of the pregnancy physiology [2, 3].

Approximately 70 to 80% of the varicose veins appear in the first trimester, when the role of the mechanical factors is insignificant. Smooth muscles relaxation and loosening of collagen fibers, a phenomenon which corresponds to progesterone and estrogen level, can cause the development of varicose veins, venous thrombosis and venous insufficiency [4]. Estrogens cause

an increased synthesis of coagulation proteins which may result in venous thrombosis and its sequelae. The importance of the hormonal system supports the fact that in menopausal period the differences in the venous thrombosis incidence in men and women are faded [4, 5].

As already mentioned, the negative factors acting on the veins in pregnancy include increased blood volume, enlargement of the uterus, weight gain, reduced physical activity, changes in the hormonal status [6]. Additional unfavourable prognostic factors are: short intervals between pregnancies, genetic predisposition, previous venous thrombosis or venous insufficiency in the superficial and deep venous system [7]. The cesarean section is a risk factor of the venous thrombosis. It elevates this risk by 3 – 16 times [7, 8]. The physiological venous reflux is intensified in pregnancy and is associated with relaxation of the venous wall due to hormonal changes and the changes of the hemodynamic conditions, without the impairment of the venous valves [9]. This phenomenon vanishes in puerperium.

In pregnancy there is also a substantial reduction of the venous return. It is intensified at 28-29 week's gestation and reaches the peak at 36 week's gestation. After 6 weeks of puerperium the normalization of venous return is observed [2].

The aim of the study was to analyze changes within the venous system of the lower extremities during pregnancy and puerperium among pregnant women with and without symptoms of venous insufficiency in the lower limbs, diagnosed during the first visit in the first trimester. The analysis was based on the blood flow velocity measurements in selected deep veins of the lower limbs.

Materials and methods

The study included 103 pregnant women consulted at the Clinic of Vascular Disease "Calisia" in Kalisz. Three patients were excluded due to the deep vein thrombosis. The age of the patients ranged from 19 to 45 years. Venous system was evaluated

according to the clinical CEAP classification [4]. Clinical classification of chronic venous insufficiency distinguishes 6 grades of VI. Grade 0 means the absence of visible or obvious signs of venous disease. Grade 1 is diagnosed on the basis of telangiectasias (intradermal venules extended up to 1 mm) or reticular veins extension (undetectable, palpable, subcutaneous veins enlargement up to a diameter of 4 mm). Grade 2 may be recognized when varicose veins are visible (palpable subcutaneous veins generally wider than 4 mm extension). The presence of edema classify grade 3 and skin changes associated with venous disease (pigmentation, venous eczema, lipodermatosclerosis) are typical for grade 4. Grade 5 contains all above mentioned skin lesions and healed venous ulcers, whereas grade 6 is characterized by skin lesions and active venous ulcers.

The patients were divided into two groups depending on the presence or absence of venous insufficiency of the lower extremities during the first visit in the first trimester. Pregnant women with symptoms of venous insufficiency were enrolled into the study group ($n = 50$), whereas patients without signs of venous insufficiency into the control group ($n = 50$). The study was approved by the medical ethics review board of University of Medical Sciences in Poznan and all patients gave their written informed consent.

The Doppler measurements of the venous system were performed four times, i.e. between 11-14, 18-22, 28-32 week's gestation and at 6 weeks after the delivery. The measurements were performed using the General Electric Logiq 500 with linear transducer (7 to 12 MHz). In all pregnant women the physical examinations and color duplex Doppler imaging were performed in supine position with legs elevated about 15 degrees. The angle of the sampling gate did not exceed 60 degrees. The following vessels were examined: common femoral vein (CFV), superficial femoral vein (SFV) and the popliteal vein (PV). Blood flow in the superficial femoral vein was assessed 10 cm below the os of the deep femoral vein. The presence of the fresh thrombosis or post-thrombotic changes were the exclusion criteria.

Doppler examination included the measurement of the blood flow velocities in the analyzed vessels (cm/s). The veins blood flow velocity changes in the course of the pregnancy were compared in both groups. In addition, changes of these parameters in four analyzed time intervals were compared between the two groups as well.

The venous flow velocities were described as the mean value and standard deviation. The concordance of those parameters with normal distribution with Shapiro-Wilk test in the group without venous insufficiency was analyzed. T-Student test for independent variables was used for parameters consistent with the normal distribution to compare between the two groups (homogeneous variations - Leven test). When compliance with the normal distribution was not confirmed, nonparametric Mann-Whitney test was used. To compare in time, that means to compare values in the first, second, third trimester and the puerperium, in each group the test was performed separately according to the results of the test for compliance with the normal distribution. For parameters consistent with normal distribution an analysis of variation for repeated measurements ANOVA with Tukey post hoc test was used. A nonparametric Friedman test with the multiple comparisons Dunn test was used when no evidence of compliance with the normal distribution was shown.

Results

The study included 100 pregnant women divided into two groups depending on the presence or absence of VI in the first trimester. The results of the analysis are presented in Tables I, II and III.

The flow velocity in the right CFV decreased significantly in the third trimester compared to those observed in the first trimester. In the puerperium an increase of flow velocity in both groups was noted, to higher values, than those observed first time in the pregnancy. These values, however, did not differ statistically. There were also no statistically significant differences between the groups (Figure 1). Similar relationships were observed in the left CFV. Mean values of blood flow velocities in the third trimester were lower than in the right CFV. Statistically significant differences were also found in the group without VI by analyzing the velocity in the second trimester in comparison to the first examination. In the postpartum period rise in the blood flow velocity in the examined vessel was observed, and the values did not differ from those seen in the first trimester.

The measurement of the blood flow in the right SFV showed statistically significant lower values in the group with VI. These changes were observed in each of the analyzed periods of pregnancy. In both groups the velocities decreased in the second and third trimester, and these changes were statistically significant. In the postpartum period increased values were observed in both groups, and those values did not differ from those obtained in the first trimester (Figure 2). A similar sequence of velocity changes was noted in the left SFV.

The analysis of the blood flow in the right PV showed a gradual reduction of flow velocity in the second and third trimester and a gradual return to baseline in the puerperium (Figure 3). Statistically significant differences were observed in the group with VI in the second and third trimester, whereas in the group without VI the statistical significance was noticed only in the third trimester when compared to those in the first trimester. Mean velocity values in the group with VI were significantly lower than those observed in the group without VI in each of the analyzed periods. Similar relationships were noticed in the left PV. Again, the mean values of blood flow velocity were significantly lower in women with VI symptoms.

Summarizing, the reduction of the blood flow velocity in the lower limbs veins with advancing gestational age was observed. The blood flow velocities showed a similar character of changes over time in both groups, with the lowest values observed in the third trimester. In the puerperium the observed changes in the blood flow velocities returned to the baseline values found in the first trimester.

Discussion

Changes of blood flow during pregnancy are likely to play an important role in the pathophysiology of venous thromboembolic events in pregnancy and puerperium [3, 10, 11, 12]. The dilatation of the veins can cause the endothelial damage, the exposure of collagen fibers and the activation of a cascade of coagulation factors leading to the formation of blood clots. The observed changes during pregnancy appear to be reversible, at least partially, because some of the analyzed parameters return to values observed in early pregnancy. This applies mainly to the velocity of the blood flow in veins. The analysis of blood flow velocity

Table I. Blood flow velocity assessment in the tested vessels in subsequent periods of the pregnancy and puerperium.

Velocity (cm/s)		I trimester			II trimester			III trimester			Puerperium		
	side	VI (-)	VI (+)	P	VI (-)	VI (+)	P	VI (-)	VI (+)	P	VI (-)	VI (+)	P
CFV (cm/s)	R	22,1 +/- 2,8	22,0 +/- 2,5	0,9171	21,2 +/- 2,6	21,9 +/- 2,5	0,1498	19,8 +/- 2,7	20,6 +/- 2,7	0,1275	22,5 +/- 2,5	22,6 +/- 2,4	0,8091
	L	22,6 +/- 2,9	22,7 +/- 1,8	0,9040	20,6 +/- 3,0	22,1 +/- 2,2	0,0243	18,7 +/- 3,1	19,6 +/- 2,8	0,0955	22,5 +/- 2,4	22,8 +/- 2,3	0,6288
SFV (cm/s)	R	18,7 +/- 3,0	15,7 +/- 3,6	0,0021	16,6 +/- 3,5	13,9 +/- 3,4	0,0024	15,9 +/- 3,2	12,7 +/- 3,4	0,0001	18,1 +/- 3,5	15,1 +/- 3,6	0,0017
	L	19,0 +/- 2,9	16,0 +/- 3,2	0,0004	17,1 +/- 3,1	13,7 +/- 3,1	0,0006	16,0 +/- 3,2	11,9 +/- 3,6	0,00001	18,3 +/- 3,5	15,4 +/- 4,0	0,0023
PV (cm/s)	R	16,9 +/- 3,9	13,3 +/- 3,9	0,0006	15,8 +/- 4,3	11,5 +/- 3,6	0,0001	10,1 +/- 3,4	10,1 +/- 3,4	0,0012	16,9 +/- 3,9	13,8 +/- 3,8	0,0019
	L	17,4 +/- 4,4	13,8 +/- 3,5	0,0003	15,5 +/- 3,9	11,5 +/- 3,5	0,0009	12,4 +/- 3,3	9,4 +/- 3,3	0,0004	17,0 +/- 3,8	14,1 +/- 3,8	0,0027

The t-Student test for independent variables.

CFV – common femoral vein, SFV – superficial femoral vein, PV – popliteal vein, VI – venous insufficiency, R- right, L – left, p – level of statistical significance

Table II. The assessment of blood flow velocity changes in the tested vessels in patients without venous insufficiency in comparison to the first trimester.

Velocity (cm/s)	side	I trimester	II trimester	III trimester	Puerperium	p	
CFV	R	22,1±2,79 17-27	21,2±2,63 17-27	19,8±2,69 16-26	22,5±2,55 17-26	I-II I-III I-P	0,1614** 0,0001* 0,8083**
	L	22,6±2,88 16-28	20,6±3,01 15-26	18,7±3,13 13-26	22,5±2,42 18-26	I-II I-III I-P	0,0050* 0,00001* 0,9977**
SFV	R	18,7±2,99 14-24	16,6±3,50 6,5-22	15,9±3,17 7-22	18,1±3,46 11-23	I-II I-III I-P	0,0001* 0,0001* 0,6097**
	L	19,0±2,90 13-26	17,1±3,10 10-22	16,0±3,16 9-22	18,3±3,45 11-24	I-II I-III I-P	0,0020* 0,0001* 0,4628**
PV	R	16,9±3,92 7-23	15,8±4,25 7-23	13,4±4,21 6-23	16,9±3,94 6-23	I-II I-III I-P	0,1105* 0,0001** 0,9998*
	L	17,4±4,37 6,8-26	15,5±3,95 7-22	12,4±3,29 5,2-19	17,0±3,77 7-22	I-II I-III I-P	0,0017* 0,0001* 0,8464**

* the ANOVA variations analysis of the data repeated with post hoc Tukey's test; ** the non-parametric Friedman test with the multiple comparisons Dunn's test; CFV – common femoral vein, SFV – superficial femoral vein, PV – popliteal vein, VI – venous insufficiency, R- right, L – left, p – level of statistical significance, I – the first trimester, II – the second trimester, III – the third trimester, P – puerperium

Table III. The assessment of blood flow velocity changes in the tested vessels in patients with venous insufficiency in comparison to the first trimester.

Velocity (cm/s)	side	I trimester	II trimester	III trimester	Puerperium	p	
CFV	R	22,0±2,47 12-27	21,9±2,55 11-26	20,6±2,71 12-26	22,6±2,41 12-26	I-II I-III I-P	0,9087** 0.0001* 0,1357**
	L	22,7±1,83 18-26	22,1±2,22 18-27	19,6±2,79 14-26	22,8±2,29 18-27	I-II I-III I-P	0,3862** 0.0001* 0,9468**
SFV	R	15,7±3,56 6-20	13,9±3,39 6-19	12,7±3,35 5,5-19	15,1±3,61 6-20	I-II I-III I-P	0.001* 0.001* 0,3177**
	L	16,0±3,17 8-22	13,7±3,13 6-20	11,9±3,57 5-21	15,4±4,02 8-25	I-II I-III I-P	0.0012* 0.0018* 0,5507**
PV	R	13,3±3,95 6-21	11,5±3,6 5-18	10,1±3,37 5-18	13,8±3,84 6-20	I-II I-III I-P	0.0001* 0.0001* 0,3286**
	L	13,8±3,50 7-20	11,5±3,55 5-20	9,4±3,27 4-17	14,1±3,81 7-20	I-II I-III I-P	0.0013* 0.0001* 0,8399**

* the non-parametric Friedman test with the multiple comparisons Dunn's test; ** the ANOVA variations analysis of the data repeated with post hoc Tukey's test; CFV – common femoral vein, SFV – superficial femoral vein, PV – popliteal vein, VI – venous insufficiency, R – right, L – left, p – level of statistical significance, I – the first trimester, II – the second trimester, III – the third trimester, P – puerperium

in the tested vessels showed that the velocity of blood flow was statistically lower in the group with venous insufficiency in the SFV and PV in all analyzed periods. In the majority of the cases, there was a substantial reduction of velocities in the third trimester in both groups, when compared to the values observed in the first trimester. These velocities increased during the postpartum period and did not differ from those observed in the first trimester in the group with and without venous insufficiency. A similar trend of changes in the CFV, SFV and PV was found by Macklon et al. when analyzing the blood flow in the veins of the lower limbs in the group of 24 healthy pregnant women [12]. Blood flow velocities in the CFV decreased from the first trimester to parturition, then an increase in the blood flow velocities was noticed. The observed changes on the left side were significantly more pronounced than those on the right side. A similar trend was also observed in the PV and SFV, but in the last no statistically significant differences were found. The observed trend of decreasing blood flow velocities in all analyzed vessels was similar to that presented in our study. However, in contrast to Macklon et al., we found the greatest changes in the SFV and PV. This remarkable reduction in blood flow velocities may result from changes in the vascular wall elasticity, which increases with advancing gestational age [13]. The result of a relative reduction in the blood flow is the blood stasis. In addition, a significant increase in the vein diameter in pregnancy may cause damage to the endothelium, exposure of collagen within the damaged vessel wall and activation of coagulation, and an excessive elongation and stretching of endothelial cells can activate venous thrombosis [14]. That is why so significant dilatation of the CFV during pregnancy may create favorable conditions for the clot formation in this area, better than in the subsequent sections of the venous sys-

tem of the lower limbs. This is consistent with the observations of other authors who suggest that in contrast to non-pregnant women, changes in the venous system of the CFV in pregnancy may predispose to thrombosis formation there, and not, as it takes a place in non-pregnant women within the shin [12]. Macklon et al. demonstrated also the impact of the test position on the blood flow velocity and width changes [12]. Authors presented that the blood flow velocity on the left side was significantly lower if the test was performed in a supine position. Changing position on the left side affected the width of the examined veins, and the blood flow velocity.

Many studies have shown a significant effect of the uterine pressure on the inferior vena cava in the supine position in an advanced pregnancy [15]. In some cases the total occlusion was observed, and the venous blood flow was preserved due to lumbar veins. Switching position to the left side is recommended in pregnancy to protect from the inferior vena cava syndrome. The data presented by the authors suggest that changing the position by a pregnant woman enhances the venous return by changing the compression of the inferior vena cava by the pregnant uterus [12]. The analysis of blood flow velocity in the selected vessels showed an increase in blood flow similar to those observed in the first trimester in all analyzed vessels. The presented study proved no statistically significant differences between mean values observed in the first trimester and at 6 weeks postpartum in both groups. Therefore, one may conclude that the changes in the blood flow velocities in the tested vessels were reversible. Moreover, there were lower values of the mean blood flow velocities in the postpartum period in the VI group, and statistical significance was observed for the SFV and PV. These results support the hypothesis of worse blood flow conditions in VI

group, what may also increase the risk of venous thromboembolic events. A similar increase in the blood flow velocity in these vessels was noted by the other investigators [12], but statistical significance was found only in the CFV. Other authors, with Baumann et al. among, showed a reduced blood flow velocity in the femoral veins in pregnancy compared to those observed after birth [16]. The increase in venous pressure resulting from compression of the inferior vena cava caused by the pregnant uterus may be responsible for the observed changes. It may also cause the dilatation of the blood vessels, eg. saphenous vein and that changes were observed in the pletyzmographic studies described by Rabhi et al. [17]. This paper demonstrated the appearance of significant changes within the venous system during pregnancy. Most of them were reversible and returned to the state before pregnancy during the puerperium [17]. The observed widening of the saphenous veins and the reduction of the capacity of the leg vessels suggested that the increase in venous pressure may cause excessive widening of veins and the reduction of their vulnerability. The compression of the inferior vena cava and an increase in intra-abdominal venous pressure are probably the two primary causes of an increased venous pressure in the legs. Reduction of the blood flow velocity on the one hand and the blood rheological changes associated with increased levels of fibrinogen on the other hand, increase the aggregation of red blood cells. These changes may cause an increase in blood echogenicity, which are the physiological changes and should not be misinterpreted as a sign of venous thrombosis [17].

Changes in venous system in pregnancy were also showed by Calderwood [10]. The assessment of the lower limbs veins in a group of 25 pregnant women at 15, 28, 36 from 39 to 41 week's gestation and on the 2nd day and 6 weeks after the delivery showed a progressive increase in the width of the CFV in both lower limbs. Calderwood, analyzing blood flow velocity in the CFV, found a significant decrease in the flow velocity with the lowest values observed around 40 week of gestation. In the puerperium the blood flow velocity increase was noticed, and the values at 6 weeks postpartum were higher than those observed at 15 week's gestation [10]. In the presented study a similar phenomenon of decreasing blood flow velocities was found. The lowest values in the third trimester and the velocity increase during the postpartum period in the CFV were noticed.

The spectral and color Doppler are the first-line methods of the venous system assessment in pregnancy, especially in suspicion of deep vein thrombosis [12]. The knowledge of physiological changes that occur in the venous system during pregnancy is extremely important because it enables the differential diagnosis of various venous system diseases.

The changes of the blood flow velocity suggest that six weeks is enough, to allow a full return of the venous system velocities to the baseline. This observation appears to be extremely important in terms of the development of thromboembolism and has important implications for the length of the use of thromboprophylaxis. An increased risk clearly exists at least six weeks after childbirth, and perhaps longer.

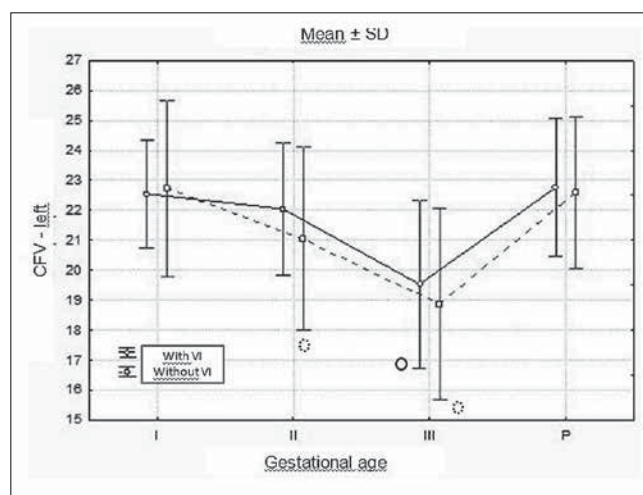


Figure 1. Blood flow velocity in the left common femoral vein (cm/s).

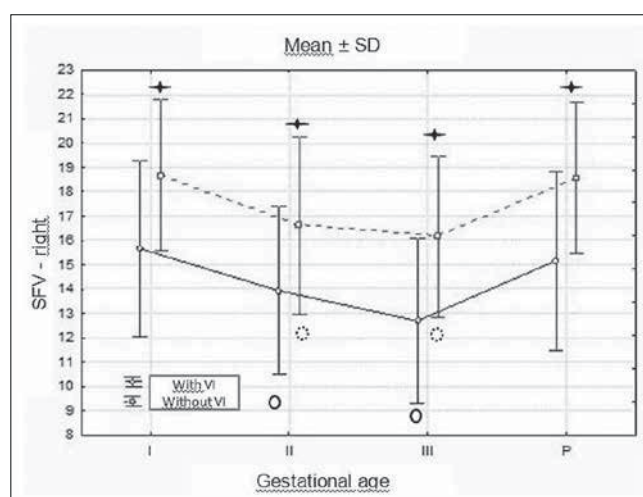


Figure 2. Blood flow velocity in the right superficial femoral vein (cm/s).

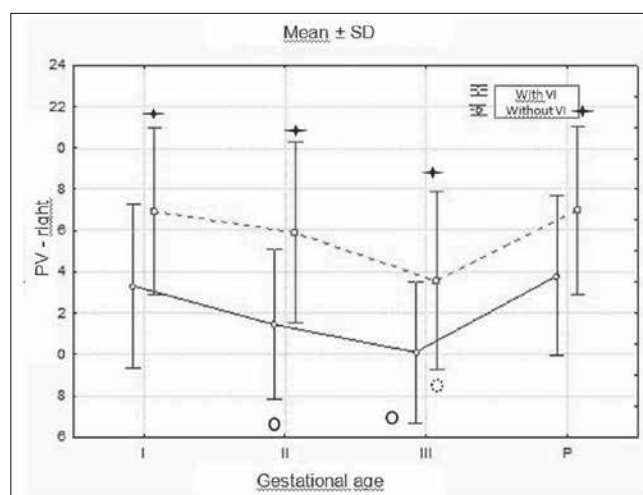


Figure 3. Blood flow velocity in the right popliteal vein (cm/s).

Figures:

- ★ Statistically significant difference between the groups.
- Statistically significant difference in the group with the VI compared to the first trimester flow.
- ⊗ Statistically significant difference in the group without the VI compared to the first trimester flow.

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